UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,174	11/26/2003	Katrin Kneipp	M0925.70114US01	5755

7590 12/02/2005

Timothy J. Oyer, Ph.D.
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
HINES, JANA A	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 12/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,174	KNEIPP ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *188-195 and 198* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/11, 8/29, 9/8/* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-17,23-37,39,43-58,60,64-72,78-85,87,91-117,130,132-135,138,139,146,147,153,155-157,159-162,164,172,179,180,182,183 and 187-198.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-17,23-37,39,43-58,60,64-72,78-85,87,91-117,130,132-135,138,139,146,147,153,155-157,159-162,164,172,179,180,182,183,187,196 and 197.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group S in the reply filed on August 29, 2005 is acknowledged. The traversal is on the ground(s) that there would not be a burdensome search. This is not found persuasive because the inventions are distinct and unrelated, each from the other because of the reasons previously provided. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Therefore as previously discussed the inventions are distinct and unrelated.

Applicants' argue that there would be no serious burden on the Examiner to search for the other groups. However, in the instant case these inventions are unrelated and distinct. The methods are distinct as claimed because they are drawn to measuring or performing different activities. Furthermore the distinct steps and products require separate and distinct searches. The groups have a separate status in the art as shown by their different classification. As such, it would be burdensome to search the inventions of groups together. Furthermore, a search for the invention of the groups would not be coextensive because a search indicating the process of one is novel or unobvious would not extend to a holding that the process of the other is novel or unobvious. Because of the different classifications of each group based upon the distinct method steps, a serious burden is imposed on the examiner to perform a complete search of the defined areas in both the patent and non-patent literature.

Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden on the examination of this application. The requirement is still deemed proper and is therefore made FINAL.

Amendment Entry

2. The amendment filed August 29, 2005 has been entered. Claims 1-2, 6-7, 19, 23-24, 29-31, 35, 39, 44-47, 49-51, 60, 64-65, 67, 72, 74, 78, 81, 87, 91-94, 99, 107, 111, 122, 125, 126, 128, 130, 134-135, 138-139, 146, 153, 155-156, 162, 172, 179-180, 190-194 have been amended. Claims 196-198 have been newly added. Claims 1-17,23-37,39,43-58,60,64-72,78-85,87,91-117,130,132-135,138,139,146,147,153,155-157,159-162,164,172,179,180,182,183, 187 and 196-197 have been withdrawn from consideration. Claims 18, 20-22, 38, 40-42, 59, 61-63, 73, 75-77, 86, 88-90, 118-121, 123-134, 127, 129, 131, 136-137, 140-145, 148-152, 154, 158, 163, 165-171, 173-178, 181, 184-186 have been cancelled. Claims 188-195 and 198 are under consideration in this office action.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 188-195 and 198 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method comprising: a) removing one or more labeled nucleotides from a nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, or uracil; b) identifying each of the one or more nucleotides by SERS and/or surfaced SERRS; and c) determining the sequence of the nucleic acid.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude, "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gostelli*, 872 F.2d 1008, 1012,

10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.,* 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Furthermore, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.,* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that

encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In *Gostelli,* the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli,* 872 F.2d at 1012, 10 USPQ2d at 1618. In this case, the specification teaches only the detection of a single analyte and fails to describe the determination of a nucleic acid sequence.

There is no disclosure of a method comprising: a) removing one or more labeled nucleotides from a nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, or uracil; b) identifying each of the one or more nucleotides by SERS and/or surfaced SERRS; and c) determining the sequence of the nucleic acid. The specification fails to provide method steps for determining the sequence of a nucleic acid sequence or using labeled thymine, adenine, cytosine, guanine, or uracil to determine the sequence. Moreover, there is description of a sequence determined by SERS or SERRS. There is no description of any method as instantly claimed. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. Moreover, the specification lacks a sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples.

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention. In view of these considerations, a person

skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of a method comprising: a) removing one or more labeled nucleotides from a nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, or uracil; b) identifying each of the one or more nucleotides by SERS and/or surfaced SERRS; and c) determining the sequence of the nucleic acid. Therefore the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

5. Claims 188-195 and 198 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Neither the specification nor originally presented claims provides support for a method comprising: a) removing one or more nucleotides from a nucleic acid; identifying each of the one or more nucleotides by Raman spectroscopy; and c) determining the sequence of the nucleic acid. The dependant claims are drawn to the nucleotides being labeled with a Raman label, and the nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, uracil and the nucleotides are identified by surface enhanced Raman spectroscopy (SERS) and/or surfaced enhanced resonance Raman spectroscopy (SERRS).

Applicant did not point to support in the specification for the instantly claimed method or the dependant claims. Moreover, applicant failed to specifically point to the

identity of a method comprising: a) removing one or more labeled nucleotides from a nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, or uracil; b) identifying each of the one or more nucleotides by SERS and/or surfaced SERRS; and c) determining the sequence of the nucleic acid. Thus, there appears to be no teaching of the claimed method. Applicant has pointed to pages 10 and 15 for support of claim 188. However the instant specification at page 10, lines 13-17 is drawn to aggregates and other surfaces which produce a very strong electromagnetic field enhancement and not to the instantly claimed method. Thus, it appears that the entire specification appears to fail to recite support for the newly method. Therefore, it appears that there is no support in the specification. Therefore, applicants must specifically point to page and line number support for the identity of a method comprising: a) removing one or more labeled nucleotides from a nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, or uracil; b) identifying each of the one or more nucleotides by SERS and/or surfaced SERRS; and c) determining the sequence of the nucleic acid as recited by the newly added claims.

Furthermore, the amendment of September 29, 2004 refers to support being found in application 10/099,287 and 10/108,128, however these applications are unrelated to the instant family of applications. Therefore it is unclear how support can be shown thru these applications. Moreover, the amendment states that support for claims 190-194 can be found on page 25,lines 27-28 yet the instant specification only has 23 pages. Therefore clarification is required to point out support for the claims in the instant

application. Therefore, the new claims incorporate new matter and are accordingly rejected

6. Claims 188-195 and 198 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 188 is rejected because it lacks a stated goal which should be recited in the preamble. A preamble should comprise a general description of all the elements or steps of the claimed invention. Furthermore, claim 188 recites the limitation "the sequence" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 188 is drawn to a method comprising: a) removing one or more nucleotides from a nucleic acid; identifying each of the one or more nucleotides by Raman spectroscopy. However, if the nucleic acid is only a single purine or pyrimidine nucleotide than it is unclear how one of skill in the art can remove multiple nucleotides from the single (a) nucleic acid. Therefore, clarification is required to overcome the rejection.

8. Claims 190-195 are drawn to the method wherein the nucleic acid comprises labeled thymine, adenine, cytosine, guanine or uracil. It is unclear when the nucleic acids became labeled. It is also unclear how the nucleic acid unidentified sequence will already comprise a labeled thymine, adenine, cytosine, guanine or uracil. Therefore, clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 188-195 and 198 are rejected under 35 U.S.C. 102(b) as being anticipated by Graham et al., (WO 97/05280 published February 13, 1997).

The claims are drawn to a method comprising: a) removing one or more nucleotides from a nucleic acid; identifying each of the one or more nucleotides by Raman spectroscopy; and c) determining the sequence of the nucleic acid. The dependant claims are drawn to the nucleotides being labeled with a Raman label, and the nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, uracil and the nucleotides are identified by surface enhanced Raman spectroscopy (SERS) and/or surfaced enhanced resonance Raman spectroscopy (SERRS).

Graham
~~Watson~~ et al., teach detection of a nucleic acids and nucleic acid units using surface enhanced raman scattering (SERS) or surface enhanced resonance raman scattering (SERRS). The invention teaches a method for sequencing a nucleic acid sequence which comprises detecting at least one target nucleotide or sequence of nucleotides within the acid (page 53, para3). The target nucleic acid may be DNA or RNA, nucleotides, nucleosides, nucleotide or nucleoside analogues or an individual nucleobase (page 15, para. 1-3). Suitable SER(R)S labels include any material capable

of generating a SERS or SERRS raman spectrum when illuminated (page 16, para. 2-3). Pages 16-17 discloses a wide variety of labels which meet the instant claim limitations. Thus, the art teaches that nucleic acids comprising labeled thymine, adenine, cytosine, guanine, and uracil which are identified by SERS. Other steps in such a sequence method may be entirely conventional; the skilled person will readily be able to make use of the data from the method in order to reach a conclusion as to an overall sequence (page 53, para. 3). In this method the SER(R) S-active label may be complexed to the relevant target nucleotide (page 53, para. 3). The labeled products can be detected by SERS or SERRS spectroscopy (page 54, para. 3). Example 9 teaches formats for assays and sequencing techniques wherein the DNA and RNA are referred to as target nucleic acids however other types of nucleic acids would be treated in the same way (page 80, para.3). The steps teach that the DNA is cleaved via restriction digest (page 81), just as required by the claims.

Therefore ~~Watson~~ Graham et al., teach a method comprising: a) removing one or more nucleotides from a nucleic acid via cleavage techniques; identifying each of the one or more nucleotides by Raman spectroscopy; and c) determining the sequence of the nucleic acid. Moreover, the prior art teaches that the nucleotides are labeled with a Raman label, and the nucleic acid comprising a labeled thymine, adenine, cytosine, guanine, and uracil are identified by SERS or SERRS.

Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Cotton et al., teach application of surface enhanced raman spectroscopy to purines and pyrimidines and related compounds. The Physics News Update, (February, 1997) teach surface enhanced raman scattering where single molecule detection is used for DNA sequencing. Graham et al., teach selective detection of deoxyribonucleic acid at ultralow concentrations by SERRS. Kneipp et al., (1994) teach Near-Infrared Surface-Enhanced Raman Scattering (NIR SERS) which detects with high sensitivity DNA based adenine. Nie et al., teach probing single molecules by surface-enhanced Raman scattering. Vo-Dinh (US Patent 5,306,403) teaches raman-based SER(R)S analysis systems for DNA sequence mapping.

Conclusion

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines

November 5, 2005

ROBERT A. ZEMAN
PATENT EXAMINER